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Maximilian Y. Emmert

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Maximilian Y. Emmert, Sacha P. Salzberg, Burkhardt Seifert, Ulrich P. Schurr, Dragan Odavic, Oliver Reuthebuch and Michele Genoni

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Institutional report - Coronary

Despite modern off-pump coronary artery bypass grafting women fare worse than men☆

Maximilian Y. Emmert[a,b,1], Sacha P. Salzberg[a,b,1,*], Burkhardt Seifert[c], Ulrich P. Schurr[b], Dragan Odavic[b], Oliver Reuthebuch[b], Michele Genoni[b]

[a]Department of Cardiac and Vascular Surgery, University Hospital Zurich, Zurich, Switzerland
[b]Department of Cardiac Surgery, Stadtspital Triemli, Zurich, Switzerland
[c]Biostatistics Unit, Institute of Social and Preventive Medicine, University of Zurich, Zurich, Switzerland

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Abstract

Female gender is an established risk factor for worse outcomes after cardiac surgery. Avoiding cardiopulmonary bypass (CPB) for coronary bypass grafting has an unknown effect on gender differences. Herein, we evaluate if gender has an impact on outcomes after modern off-pump coronary artery bypass grafting (OPCAB). From 2002 to 2007, we analyzed 983 patients (male: $n=807$/female: $n=176$) who underwent OPCAB with symptomatic multi-vessel disease at our institution. The link between gender and outcome was assessed by multivariate analysis and logistic regression. A composite endpoint was constructed from: 30-day-mortality, renal failure, prolonged intensive care unit (ICU) stay, neurological complications, use of intra-aortic balloon pump (IABP) and conversion to CPB. Mortality was 3.2% in women vs.1.8% in men ($P=0.15$) and the EuroSCORE was significantly correlated to gender (6.8 vs. 5.2; $P<0.001$), even after correction ($P=0.036$). Significant more occurrence of the composite endpoint was noted in women (39.8% vs. 29.0%; $P=0.007$) whereas for men the risk was much lower [odds ratio (OR) 0.65; 95% confidence interval (CI) 0.46–0.92; $P=0.015$]. For both genders the logistic regression revealed a risk increase of 15% per one-point-increase of EuroSCORE (corrected) (OR 1.15; 95% CI: 1.10–1.19; $P<0.0001$). Women had more frequently a prolonged stay at ICU ($P=0.006$) and had a higher stroke rate (2.3% vs. 1.2%; $P=0.29$). Complete revascularization was achieved similarly (95% vs. 94%; $P=0.93$). OPCAB offers low mortality and excellent clinical outcome. Women are more likely to experience postoperative complications. Even if partially neutralized by avoiding CPB, gender differences remain present with modern OPCAB strategies.

Keywords: Coronary heart disease; Gender differences; Off-pump surgery

1. Introduction

Coronary artery disease (CAD) is the leading cause of mortality in women [1] (American Heart Association/www.women.americanheart.org). Surgical revascularisation for CAD remains the treatment of choice in patients with three-vessel disease, left-main-disease, associated decreased left ventricular function and diabetes mellitus [2–4]. Current data report the mortality rate after coronary artery bypass grafting (CABG) to be significantly increased in females [5, 6]. Possible causes may be related to later clinical presentation, worse hemodynamic impairment, higher age, more incidence of diabetes, more severe heart disease and particular anatomical considerations, such as smaller vessel diameter [1]. In addition to this, women seem to suffer from increased length of intensive care unit (ICU) stay due to more frequent cardiac low-output states [6]. Furthermore, especially younger women with myocardial infarction (MI) undergoing CABG represent a particular high-risk sub-group, as reported by a higher overall mortality [5]. The EuroSCORE (www.euroscore.org) is an established score system for preoperative risk stratification in patients undergoing cardiac surgery. In this risk stratification, female gender is an independent risk factor for worse outcomes after cardiac surgery [7]. Cardiopulmonary bypass (CPB) is associated with severe complications, such as stroke, renal dysfunction, low cardiac output, post-operative bleeding and systemic inflammatory response syndrome (SIRS). Minimally-invasive approaches to CABG have led to the development of off-pump coronary artery bypass grafting (OPCAB) which permits myocardial revascularisation while avoiding CPB. OPCAB remains limited as clinical acceptance has yet to be achieved. Current data demonstrate that OPCAB is associated with less complications and a decrease in mortality [8]. These reports have not assessed the role of female gender on these outcomes. Herein, we determine if gender differences remain present in a modern OPCAB setting.

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[1]These authors contributed equally.

*Corresponding author. Department of Cardiovascular Surgery, University Hospital Zurich, Raemi Street 100, 8091 Zurich, Switzerland. Tel./fax: +41-44-255 1111.

E-mail address: sacha.salzberg@usz.ch (S.P. Salzberg).

Table 1
Preoperative demographics

Parameter	Women ($n=176$)	Men ($n=807$)	P-value
Age (years)	66±10	65±10	0.99
EuroSCORE	6.8±3.4	5.2±3.5	<0.001
EuroSCORE (corrected −1)	5.8±3.4	5.2±3.5	0.036
EF (%)	56±17	57±15	0.69
BMI (kg/m²)	27±4	27±3	0.85
History of smoking (%)	102 (58)	476 (59)	0.87
Diabetes (%)	47 (27)	194 (24)	0.38
Hypertension (%)	82 (48)	363 (45)	0.86
PAD (%)	19 (11)	89 (11)	1.00
COPD (%)	9 (5)	20 (2.5)	0.14
Positive family history (%)	60 (34)	307 (38)	0.39
Myocardial infarction (<90 days) (%)	67 (38)	323 (40)	0.79
Left main stem disease (%)	62 (35)	282 (35)	1.00
IABP preop (%)	18 (10)	73 (9)	0.89
Elective (%)	121 (68)	525 (65)	0.85
Urgent (%)	35 (20)	202 (25)	0.75
Emergent (%)	21 (12)	80 (10)	0.11
Redo surgery (%)	3 (2)	8 (1)	0.43

EF, ejection fraction; BMI, body mass index; PAD, peripheral artery disease; COPD, chronic obstructive pulmonary disease; IABP, intra-aortic balloon pump.

2. Methods

From 2002 to 2007, a total of 983 patients underwent isolated OPCAB for symptomatic multi-vessel disease (MVD) at our teaching institution. Of these patients, 82% ($n=807$) were male and 18% ($n=176$) female and preoperative risk was calculated by use of the EuroSCORE risk stratification system. A database review was performed after approval by our institutional review board (including a waiver of signed informed consent). Tables 1–3 resume patients' demographics, including EuroSCORE, co-morbidities, medication and preoperative data.

In brief, surgery was performed through a median sternotomy and heparin was administered to obtain active clotting time in excess of 300 s. Epicardial atrial and sometimes ventricular pacemaker wires were applied. An octopus (Octopus®4 Tissue-Stabilizer, Medtronic, Minneapolis, USA) was used to properly expose the target vessel. A mister blower (Guidant, Indianapolis, USA) was used to clear the operating field during anastomosis. Coronary arteriotomy was performed with a beaver blade and shunt insertion (ClearView® Intracoronary-Shunt, Medtronic, Minneapolis, USA) was attempted in all. Proximal anastomosis was performed in a clamp-less fashion using a heartstring-device (HEARTSTRING™ Seal-System, Guidant, Indianapolis, USA). Revascularization was commenced by left anterior descending-left internal mammary artery (LAD-LIMA) grafting, after which the right coronary system was approached, and finally the circumflex territory was done. Hemodynamic optimization was attempted by fluid resuscitation, Trendelenburg positioning, atrial pacing and catecholamine administration as a last measure. When still insufficient an intra-aortic balloon pump (IABP) was placed intra-operatively ($n=10$, 1%). As an ultimate action, or if necessary, conversion to CPB was done ($n=57$; 6%). A beating-heart procedure was attempted; only in difficult cases cardioplegic arrest was performed.

Continuous data are presented as mean±standard deviation (S.D.) and are compared using the Mann–Whitney test. Categorical data are presented as number and percentage and are compared using the χ^2-test or Fisher's exact test where appropriate. A 'Completeness of Revascularization Index' (CRI) was calculated for each patient and was defined as the total number of distal grafts divided by the number of the affected coronary vessels reported on the preoperative coronary angiogram. A composite endpoint was constructed from: 30-day-mortality, postoperative renal failure, ICU length of stay (LOS) (>2 days), neurological complications, use of IABP and conversion to CPB. A

Table 2
Preoperative medication

Parameter	Women ($n=176$)	Men ($n=807$)	P-value
Heparin (%)	30 (17)	177 (22)	0.15
Aggrastat (%)	26 (15)	145 (18)	0.51
Clopidogrel (%)	16 (9)	57 (7)	0.65
Acetyl salicyl acid (%)	157 (89)	747 (93)	0.65
Others (%)	11 (6)	48 (6)	1.00
ACE inhibitors (%)	26 (15)	121 (15)	1.00
Beta blocker (%)	53 (30)	234 (29)	0.93

Table 3
Preoperative laboratory values

Parameter	Women ($n=176$)	Men ($n=807$)	P-value
Lc ($10^3/\mu l$)	8.2±5.6	8.0±3.6	0.65
Hb (g/dl)	13.9±1.7	13.8±1.7	0.58
Hk (%)	40.5±4.8	40.5±1.7	0.99
Tc ($10^3/\mu l$)	266±76	252±71	0.06
Chol (mmol/l)	4.8±1.3	5.2±13.4	0.47
HDL (mmol/l)	1.2±0.3	1.2±0.4	0.80
Tg (mmol/l)	2.0±1.7	1.8±1.5	0.86
CRP (g/l)	12±26	11±26	0.66
Crea (μmol/l)	86±23	88±39	0.77
BNP (ng/l)	281±756	233±464	0.16
Trop T (μg/l)	2.0±7.0	2.4±10.9	0.54
CK (IU/l)	157±294	141±268	0.22
CK-MB (IU/l)	23±32	26±66	0.84

Lc, leukocytes; Hb, haemoglobin; Hk, Haematocrit; Tc, thrombocytes; Chol, Cholesterine; HDL, high-density lipoprotein; Tg, triglycerides; CRP, C-reactive protein; Crea, creatinine; BNP, B-type natriuretic peptide; Trop T, troponin T; CK, creatine-kinase; CK-MB, creatine-kinase MB.

Table 4
Composite endpoint and postoperative data

Parameter	Women (n=176)	Men (n=807)	P-value
Composite endpoint (%)	70 (39.8)	234 (29.0)	0.007
Mortality (%)	6 (3.4)	14 (1.7)	0.15
IABP intra-operative (%)	1 (0.6)	9 (1.1)	0.44
CPB conversion (%)	9 (5.1)	48 (5.9)	0.86
Neurological events (central) (%)	4 (2.3)	10 (1.2)	0.29
Neurological events (peripheral) (%)	1 (0.6)	7 (0.9)	1.00
Re-thoracotomy (%)	8 (4.5)	27 (3.3)	0.50
Postoperative creatinine (>220 μmol/l) (%)	1 (0.6)	8 (1.0)	0.51
LOS ICU (>2 days) (%)	48 (27.3)	144 (17.8)	0.006
Ventilation time (h)	12.9±20.8	12.1±13.5	0.30
LOS ICU (days)	2.7±4.9	2.1±3.5	0.011
LOS in-hospital (days)	10.1±5.2	10.2±5.3	0.12
Hb (g/dl) (1 day)	10.0±1.4	9.9±1.3	0.50
Hk (%) (1 day)	29.5±4.3	29.0±3.9	0.29
Lc (10^3/μl) (1 day)	10.0±3.7	9.9±4.3	0.26
Tc (10^3/μl) (1 day)	164±87	182±111	0.037
CK (IU/l) (1 day)	449±559	442±462	0.73
CK-MB (IU/l) (1 day)	27±42	28±42	0.49
Trop T (μg/l) (1 day)	4.4±17.4	5.6±18.7	0.17
Crea (μmol/l) (1 day)	85±25	89±47	0.73

IABP, intra-aortic balloon pump; CPB, cardiopulmonary bypass; LOS, length of stay; ICU, intensive care unit; Lc, leukocytes; Hb, haemoglobin; Hk, haematocrit; Tc, thrombocytes; Crea, creatinine; Trop T, troponin T; CK, creatine-kinase; CK-MB, creatine-kinase MB.

bivariate logistic regression with gender and a gender corrected EuroSCORE as covariates was performed to analyze whether gender is an independent predictor of the composite endpoint. All analyses were performed using SPSS13 (SPSS Inc, Chicago, IL, USA). Two-sided P-values <0.05 are considered statistically significant.

3. Results

The mortality was 2% for all-comers. Females were more likely to die during the first 30 days when compared to males (3.4% vs. 1.7%; P=0.15). Women appeared to have a higher occurrence of stroke than men (2.3% vs. 1.2%; P=0.29) whereas the rate of peripheral neurological complications was similar in both groups (0.6% vs. 0.9%; P=1.00). Furthermore, the frequency of re-operation for bleeding was higher in women, although this did not reach statistical significance (4.5% vs. 3.3%; P=0.50). In contrast to this, it appeared that women experienced a significant longer stay in the ICU when compared to males (2.7±4.9 days vs. 2.1±3.5 days; P=0.011), whereas the length of hospital stay was quite similar (10.1±5.2 days vs. 10.2±5.3 days; P=0.12). Additionally, it became apparent that women had a significantly lower level of platelets than men (164±87 vs. 182±111; P=0.037) at the first postoperative day (Table 4).

Intra-operative insertion of an IABP was necessary in (0.6% vs. 1.1%; P=0.44). The rate of conversion to CPB during the procedure was 5.1% vs. 5.9%; P=0.86, after conversion 78% vs. 75% were performed beating heart, while 22% vs. 25% underwent aortic cross-clamping. The number of the diseased coronary vessels were well comparable (2.76±0.49 vs. 2.79±0.50; P=0.64). Next, the number of arterial grafts per patient (1.76±1.05 vs. 1.69±0.94; P=0.52), the number of saphenous vein grafts (SVG) per patient (1.87±1.25 vs. 1.97±1.27; P=0.29) and the total number of used grafts per patient were similar among both genders (3.63±1.03 vs. 3.66±0.96; P=0.75). In addition to this, completeness of revascularization was achieved in 95% of women vs. 94% of men (P=0.93) and the CRI revealed no significant differences (1.39±0.67 vs. 1.40±0.63; P=0.90) (Table 5).

The EuroSCORE for women was significantly higher than in men (6.8±3.4 vs. 5.2±3.5; P<0.001). Even the corrected EuroSCORE (EuroSCORE −1) for female gender was still significantly higher than in men (5.8±3.4 vs. 5.2±3.5; P=0.036).

Significantly more occurrence of the composite endpoint was noted in 40% vs. 29% for women and men (P=0.007). These results were mainly driven by the significant longer stay (>2 days) at the ICU (27% vs. 18%; P=0.006). Although the mortality rate (3.4%), the number of central neurological complications (2.3%) and the frequency of re-thoracotomy (4.5%) were higher in women, these components failed to reach statistical significance (Table 4). Mean EuroSCORE (corrected −1) of the affected women was 7.3±3.8 (median: 7; range: 0–17) vs. 6.3±4.0 (median: 5, range: 0–18) in men. In the non-affected the EuroSCORE was similar: 4.8±3.0 (median: 4, range: 0–20) vs. 4.7±3.1 (median: 4; range: 0–18) (Fig. 1).

Female gender was an independent risk factor, as men had a significantly lower risk for the occurrence of our composite endpoint. The odds ratio (OR) was 0.65 (95% confidence interval (CI): 0.46–0.92; P=0.015). The logistic regression for both genders revealed a significant risk increase of 15% per one-point-increase of EuroSCORE (corrected). The OR was 1.15 (95% CI: 1.10–1.19; P<0.0001). Taken together, these data suggest that a male with a EuroSCORE of four points might roughly correlate with a

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Table 5
Intraoperative data

Parameter	Women (n=176)	Men (n=807)	P-value
CPB conversion (%)	9 (5.1)	48 (5.9)	0.86
CPB time (min)	93±22	89±27	0.74
Aortic x-clamp time (min)	60±16	58±21	0.69
Arterial grafts per patient	1.76±1.05	1.69±0.94	0.52
LIMA (%)	167 (94.9)	791 (98.0)	0.42
RIMA (%)	83 (47.2)	363 (44.9)	0.62
Radial artery (%)	23 (13.0)	97 (12.0)	0.44
SVG per patient	1.87±1.25	1.97±1.27	0.29
Use of SVG (%)	144 (81.8)	653 (80.9)	0.56
Total number of grafts per patient	3.63±1.03	3.66±0.96	0.75
Number of diseased vessels	2.76±0.49	2.79±0.50	0.64
Completeness of revascularization (%)	167 (94.9)	757 (93.9)	0.93
Completeness of revascularization index (CRI)	1.39±0.67	1.40±0.63	0.90
EC (300 ml per unit)	2.03±4.36	2.17±3.40	0.06
FFP (300 ml per unit)	1.17±2.75	1.12±2.61	0.60
TC (300 ml per unit)	0.22±0.72	0.22±0.78	0.79

CPB, cardiopulmonary bypass; LIMA, left internal mammary artery; RIMA, right internal mammary artery; SVG, saphenous vein graft; EC, erythrocyte concentrate; FFP, fresh frozen plasma; TC, thrombocyte concentrate.

female having a EuroSCORE (corrected) of two points in regard to the occurrence of our composite endpoint.

4. Discussion

In our series, it appears that OPCAB offers low mortality and excellent clinical outcomes for patients requiring myocardial revascularization. However, despite the elimination of CPB, gender differences in regard to clinical outcomes remain present and cannot be completely compensated by the avoidance of CPB. When compared to men, women are significantly more likely to experience postoperative complications, such as mortality, ICU LOS, neurological complications, re-operation for bleeding and conversion to CPB. We believe the significantly decreased postoperative level of platelets among women might be a plausible explanation

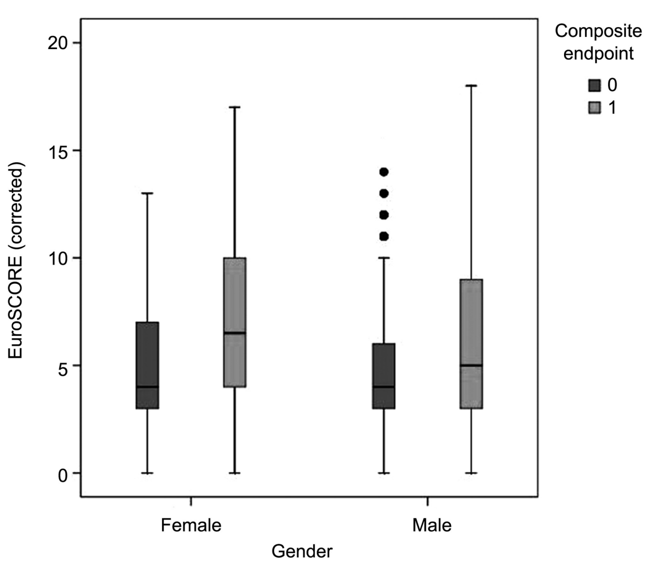

Fig. 1. Median EuroSCORE (corrected −1) of the affected women (left column, right bar) was 7 (range: 0–17) vs. 5, (range 0–18) in men (right column, right bar); mean: 7.3±3.8 vs. 6.3±4.0. In the non-affected group (left column and right column, left bar) the median EuroSCORE was similar among both genders: 4 (0–18) vs. 4 (0–20) (mean: 4.8±3.0 vs. 4.7±3.1).

when considering the higher incidence of re-operation for bleeding. In addition, these findings are clearly confirmed by a significant lower OR of 0.65 (P=0.015) for the occurrence of our composite endpoint in men.

When taking the EuroSCORE into account we found it impressive, as even after correction (EuroSCORE −1) women had a significantly higher EuroSCORE than men (P=0.036). We, and others, believe that this highlights the fact that women may actually suffer from more severe CAD and worse associated co-morbidities [9]. These co-morbidities include: age, renal function, pulmonary conditions, peripheral vascular disease, neurological dysfunction and impaired ejection fraction (EF). Furthermore, women have smaller coronary arteries adding to the operative challenge when performing OPCAB [1].

Parallel to this, attention has recently shifted towards genetic factors which may contribute to worse outcomes in women. Schuit et al. conducted a prospective cohort study on postmenopausal women. They looked at MI and ischemic heart disease (IHD) and analysed the prevalence of a specific estrogen receptor. Female heterozygous carriers of haplotype-1 had an increased risk of MI (event rate: 2.8%; relative ratio (RR) 2.23) compared with non-carriers (event rate: 1.3%), whereas homozygous carriers had an increased risk (event-rate: 3.2%; RR: 2.48). For IHD events, they observed a similar association. In women, the effect of haplotype-1 on fatal IHD was larger than on non-fatal IHD. In men, the *ESR1* haplotypes were not associated with an increased risk of MI or IHD. The authors concluded that postmenopausal women who carry the gene have not only an increased risk of having an IHD event but also an increased risk of death from such an event [10]. Regardless of the surgical approach, these results clearly indicate that women seem to have a genetic component for worse outcomes after cardiac surgery and might explain the significantly increased occurrence of our composite endpoint.

In contrast to this, Cartier and colleagues prospectively followed up 1000 OPCAB patients and found that particularly incomplete revascularization (hazard ratio (HR) 2.35), multiple internal thoracic artery (MITA) (HR: 0.61), left ventricular EF (HR: 0.19) and cerebral vascular disease (HR: 1.50) but not female sex ($P=0.89$) were significant predictors of long-term mortality. They concluded that a lower survival rate especially observed in younger women was mostly related to a higher prevalence of preoperative co-morbidity and a lesser use of MITA grafts than gender itself [5]. In regard to the long-term outcome the report also highlights the importance of completeness of revascularization which has often been reported to be limited in OPCAB [4, 11]. By help of our constructed CRI, we were able to demonstrate completeness of revascularization for both genders and could successfully exclude this important risk factor. This is in line with Puskas et al. who recently demonstrated feasibility of completeness of revascularization in OPCAB [12]. Our results may be explained by our 100% standardized OPCAB approach and especially by the fact that we perform 95% of all cases in OPCAB fashion which is far above the international average [11].

In regard to outcomes when comparing on-pump vs. off-pump CABG in women, numerous reports are available [13, 14]. Mack et al. reported outcomes on 21,902 consecutive female patients at 82 institutions undergoing isolated CABG. Propensity scoring was performed on 7376 women demonstrating 73% higher mortality ($P=0.002$) and a 47% higher risk of bleeding complications ($P=0.019$) in patients undergoing on-pump CABG. It remains unclear if the avoidance of CPB is the only mechanism involved decreasing mortality, as the risk profile is essentially the same between the matched groups reported [13].

This report clearly indicates a benefit for women undergoing OPCAB and is in line with our overall results that OPCAB offer low mortality and an excellent clinical outcome. In comparison, we focussed on the important question, if off-pump procedures do also narrow the well described gender differences after on-pump surgery. In another large retrospective study, Puskas et al. evaluated 11,413 patients (females: $n=3248$), comparing OPCAB to CABG and found that women were older and had higher predicted risk than males. Among women undergoing CABG they confirmed an increased OR for death, stroke, MI and for major cardiac adverse events (MACE). Among women, OPCAB was associated with a significant risk reduction for death, stroke and MACE. Moreover, they demonstrated that women treated with OPCAB had outcomes statistically similar to men regardless of operative strategy. The authors concluded that OPCAB is associated with fewer major adverse cardiac events, narrow gender differences and even benefits women disproportionately [15]. In contrast to these data, our results suggest that gender differences remain present after off-pump procedures. On the other hand, the univariate analysis of our composite endpoint components showed that the statistical significance was mainly driven by the longer stay at the ICU (>2 days). When excluding this factor, and as all other components failed to reach statistical significance, they might be partially comparable to their findings [15].

In conclusion, despite modern OPCAB gender differences in regard to outcomes and remain present and cannot be fully compensated by this minimally-invasive approach. Without a doubt OPCAB seems to benefit women compared to conventional on-pump CABG. However, it remains unclear to what extent off-pump procedures narrow these gender differences. Additional studies are needed to address this question, particularly since women have always been under-represented in the current data. Finally, the suggestion that genetic factors might contribute to worse outcomes in females has to be recognized and elucidated in future studies.

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eComment: Re: Despite modern off-pump coronary artery bypass grafting women fare worse than men

Authors: ***Christopher A. Efthymiou****, Leeds General Infirmary, Great George Street, Leeds LS1 3EX, UK;* ***David J. O'Regan***

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The results of Emmert et al. [1] clearly demonstrate the effect of gender on postoperative mortality and morbidity. Their analysis of 983 patients revealed the risk of mortality in females to be 1.8 times that of males. Furthermore women had a longer ICU stay, a higher stroke rate and were found to be more likely to develop postoperative complications compared to the European system for cardiac operative risk evaluation (EuroSCORE) [2]. Despite performing revascularization using an off-pump technique the groups results for mortality were significantly greater than the 1% increase calculated by the EuroSCORE. Other investigators have also found similar differences. Vaccarino et al. [3] reported in-hospital mortality rates in women younger than 50 years old three times higher than that of men. Although alluded to in the article the pathophysiology behind increased mortality in women remains unclear. Women tend to be older at the time of surgery with a greater number of co-morbidities. They have smaller coronary arteries thereby making the task of performing anastomoses more challenging. Fewer arterial grafts are performed in women, and smaller chamber volume as well as cardiac mass and circulating volume may reduce functional reserve to a greater extent compared to men.

We performed coronary revascularization on a male patient who had undergone bilateral orchidectomy during childhood for undescended testes. The patient had feminine features of peripheral obesity, lack of facial hair and gynaecomastia. He was also non-compliant with his testosterone replacement therapy. During the procedure it was noted that his coronary arteries were of a smaller diameter and fragile in nature when compared to an equivalent male patient. The hypothesis was then postulated: should this patient score an additional point on the EuroSCORE? Clearly this is a rare occurrence, but should the patient be scored as a woman?

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Routine Off-Pump Coronary Artery Bypass Grafting Is Safe and Feasible in High-Risk Patients With Left Main Disease

Maximilian Y. Emmert, MD, Sacha P. Salzberg, MD, Burkhardt Seifert, PhD, Ulrich P. Schurr, MD, Simon P. Hoerstrup, MD, Oliver Reuthebuch, MD, and Michele Genoni, MD

Department of Cardiac and Vascular Surgery, University Hospital Zurich; Department of Cardiac Surgery, Triemli Hospital Zurich; and Biostatistics Unit, Institute of Social and Preventive Medicine, University of Zurich, Zurich, Switzerland

Background. Coronary artery bypass graft surgery (CABG) remains the method of choice for patients with left main disease (LMD). The precise role of off-pump coronary artery bypass graft surgery (OPCABG) remains unclear in this setting. We report the safety and feasibility of a routine OPCABG approach to patients with LMD.

Methods. From 2002 to 2007, 983 patients underwent myocardial revascularization at our institution. We compared 343 OPCABG patients with LMD (group A) to 640 OPCABG patients without LMD (group B). The relationship between the presence of LMD and outcome in OPCABG procedures was statistically assessed. A composite endpoint (30-day mortality, postoperative renal failure, intensive care unit length of stay [>2 days], neurologic complications, use of intra-aortic balloon pump, and conversion to cardiopulmonary bypass) was also used. In addition, completeness of revascularization was compared in both groups.

Results. Group A had a lower mortality rate (1.7% versus 2.2%; $p = 0.81$), and no differences were noted in conversion to cardiopulmonary bypass (6.7% versus 5.3%; $p = 0.39$), intra-aortic balloon pump use (0.3% versus 1.4%; $p = 0.18$), and occurrence of composite endpoint (30.9% versus 30.8%; $p = 0.99$). The number of arterial grafts per patient was significantly higher among patients in group A (1.77 ± 0.95 versus 1.66 ± 0.95; $p = 0.029$) owing to the more frequent use of the right internal mammary artery (49.6% versus 42.3%; $p = 0.031$), whereas the total number of distal anastomoses (3.72 ± 0.90 versus 3.62 ± 1.01; $p = 0.28$) and complete revascularization (94% versus 95%; $p = 0.55$) were similar. Logistic regression confirmed that LMD is no risk factor for the occurrence of our composite endpoint (odds ratio 1.00; 95% confidence interval: 0.75 to 1.33; $p = 0.99$).

Conclusions. A modern OPCABG approach offers low mortality, excellent clinical outcomes, and does not come at the price of less complete revascularization in these high-risk patients.

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Left main coronary artery disease (LMD) is a well-established risk factor for cardiac-related adverse events [1–5] and is generally associated with a higher calcific load of the aorta and other peripheral arteries [6, 7]. As implemented in the commonly accepted guidelines of the American Heart Association (with a level of evidence: A), coronary artery bypass graft surgery (CABG) remains the method of choice for patients with LMD [8].

Cardiopulmonary bypass (CBP) is associated with serious complications such as low cardiac output, stroke, postoperative bleeding, renal dysfunction, and systemic inflammatory response syndrome [9, 10]. Minimally invasive techniques for CABG have led to the development of off-pump coronary artery bypass grafting (OPCABG), which permits myocardial revascularization while avoiding CPB.

Current data demonstrate that OPCABG is associated with fewer major complications and a decrease of risk-adjusted mortality in general [11–17]. However, as it is practiced today, OPCABG remains debated, as overall clinical acceptance has yet to be achieved. In addition to temporary stabilization, off-pump procedures involve repetitive mobilization of the heart, especially when the circumflex territory is addressed. In addition to this, prolonged phases of hypotension and decreased cardiac output may compromise hemodynamics [18, 19]. For these reasons, surgeons have been cautious so far to expose patients with significant LMD to these techniques, for fear of emergent conversion to CPB.

The aim of this study was to evaluate the safety and feasibility of a routine OPCABG approach to patients with LMD.

Material and Methods

Between 2002 and 2007, a total of 983 patients underwent isolated OPCABG for symptomatic coronary artery disease (CAD) at our institution. A single-center retrospective database analysis was conducted after approval by

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Address correspondence to Dr Salzberg, Department of Cardiovascular Surgery, University Hospital Zurich, Raemi St 100, Zurich 8091, Switzerland; e-mail: sacha.salzberg@usz.ch.

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our local Institutional Review Board, including a waiver of informed consent. We compared 343 OPCABG patients with LMD (group A) and 640 patients without LMD (group B). The LMD was defined as stenosis of the main stem of the left coronary artery of more than 50%. Of these patients, 81.2% (n = 799) were male and 18.2% (n = 184) were female. Surgery was performed as follows: elective (69%; n = 679), urgent (22%; n = 217) and emergent (9%, n = 87). Reoperative cases other than previous CABG were done in 1% of cases, and 9% of all patients (n = 92) required preoperative implantation of an intra-aortic balloon pump (IABP). Mean preoperative risk stratification was done by use of the European System for Cardiac Operative Risk Evaluation (EuroSCORE) risk stratification system. Table 1 and 2 summarize patient's demographics, including EuroSCORE, comorbidities, type of medication, and preoperative data.

All OPCABG procedures were performed through a median sternotomy. Internal mammary artery harvest was skeletonized, and all other grafts where endoscopically harvested (including radial artery). Cardiac exposure was obtained by four pericardial stay sutures. The pericardium was opened in a T fashion. Heparin was administered to obtain activated clotting time in excess of 300 s, and repeated if necessary. Epicardial atrial and ventricular temporary pacemaker wires were administered to all patients. Cardiac positioning was first done with rolled up surgical swabs; after this an Octopus (Octopus 4 Tissue Stabilizer; Medtronic, Minneapolis, MN) was used to properly expose the target vessel. In selected cases, the right pleural space was widely opened to allow cardiac positioning into the right side of the chest for better exposition of the circumflex artery territory. Additionally, a mister blower (Guidant, Indianapolis, IN) was used. Coronary arteriotomy was performed with a beaver blade, and shunt insertion (ClearView Intracoronary Shunt; Medtronic) was used whenever possible. Anastomosis was performed with polypropylene 8-0 suture for all arterial anastomosis and polypropylene 7-0 running suture when a venous graft was used. Proximal anastomosis was performed in a clampless fashion ("no touch" technique for proximal anastomosis) using the Heartstring device (Heartstring Proximal Seal System; Guidant) with 6-0 polypropylene. Flow was measured using the MediStim Quick Fit ultrasound probes (MediStim, Nydalen, Norway) in all cases. If insufficient flow was documented (flow <5 mL/min or pulsatility index >4) [20, 21], the anastomosis was repeated.

Surgical revascularization was started by left anterior descending to left internal mammary artery grafting. After this, the right coronary system was approached, and finally the circumflex territory was revascularized. In patients with LMD, left anterior descending and circumflex arteries were always grafted, regardless of the degree of stenosis. All other vessels with significant lesions (>70%) were identified preoperatively in the angiogram and selected as target for revascularization.

In all cases, hemodynamic optimization was attempted by volume management, Trendelenburg positioning, atrial pacing and catecholamine administration. If this conservative approach was insufficient, an IABP was inserted intraoperatively. If the patient remained unstable under IABP support, conversion to CPB was done. Before nonemergent conversion, transesophageal echocardiography and pulmonary artery catheter (Swan-Ganz catheter) analysis were used to evaluate hemodynamic instability. Emergent conversion to CPB was avoided, and a beating heart procedure was attempted whenever possible. Only in difficult cases was cardioplegic arrest performed.

Table 1. Preoperative Demographics

Variable	Group A LMD n = 343	Group B Non-LMD n = 640	p Value
Age, years	66 ± 10	65 ± 10	0.29
Male (%)	281 (82)	518 (81)	0.76
Female (%)	62 (18)	122 (19)	0.69
EuroSCORE	5.5 ± 3.6	5.5 ± 3.5	0.96
Ejection fraction, %	57 ± 15	56 ± 16	0.24
Body mass index, kg/m^2	27 ± 4	27 ± 3	0.92
History of smoking (%)	195 (57)	378 (59)	0.45
Diabetes mellitus (%)	89 (26)	154 (24)	0.48
Hypertension (%)	165 (48)	288 (45)	0.86
Peripheral artery disease (%)	38 (11)	77 (12)	0.59
COPD (%)	7 (2)	19 (3)	0.55
Positive family history (%)	127 (37)	237 (37)	1.00
Myocardial infarction, <90 days (%)	145 (42)	243 (38)	0.24
IABP preoperatively (%)	38 (11)	51 (8)	0.20
Elective (%)	199 (58)	397 (62)	0.82
Urgent (%)	96 (28)	179 (28)	0.93
Emergent (%)	48 (14)	64 (10)	0.38
Redo surgery (%)	7 (2)	6 (1)	0.20
Troponin T, μg/L	3.6 ± 11.9	1.7 ± 3.6	0.20
Creatine kinase, IU/L	185 ± 368	119 ± 182	0.57
Creatine kinase-MB, IU/L	25 ± 38	25 ± 32	0.14

COPD = chronic obstructive pulmonary disease; EuroSCORE = European System for Cardiac Operative Risk Evaluation; IABP = intra-aortic balloon pump; LMD = left main disease.

Table 2. Preoperative Medication

Medication	Group A LMD n = 343	Group B Non-LMD n = 640	p Value
Liquemin (%)	82 (24)	126 (20)	0.14
Aggrastat (%)	65 (19)	106 (17)	0.38
Plavix (%)	22 (6)	58 (9)	0.18
Aspirin (%)	319 (93)	569 (89)	0.41
Others (%)	24 (7)	34 (5)	0.32
ACE inhibitors (%)	55 (16)	93 (15)	0.58
Beta-blocker (%)	117 (34)	169 (26)	0.012

ACE = angiotensin-converting enzyme; LMD = left main disease.

Statistical Analysis

Continuous data are presented as mean ± SD and are compared using the Mann-Whitney *U* test. Categorical data are presented as number and percentage and are compared using the χ^2 test or Fisher's exact test where appropriate. A completeness of revascularization index was calculated for each patient. The completeness of revascularization index was defined as the total number of distal grafts divided by the number of the affected coronary vessels reported on the preoperative coronary angiogram. A composite endpoint was constructed from the following: 30-day mortality, postoperative renal failure, intensive care unit length of stay of more than 2 days, use of IABP, conversion to CPB, and central neurologic complications. Central neurologic complications were divided into permanent central complications such as stroke, and temporary complications (1 to 7 days) such as postoperative delirium. Logistic regression was performed to analyze whether LMD is an independent predictor of the composite endpoint. All analyses were performed using SPSS 13 (SPSS Inc., Chicago, IL). All p values less than 0.05 are assumed to be statistically significant.

Results

Demographics and Preoperative Data

Patients with LMD (group A; n = 343) and patients without LMD (group B; n = 640) were comparable in age, sex, comorbidities, cardiovascular risk factors, preoperative medication, and laboratory variables (Tables 1 and 2). Although not being significant, impaired cardiac conditions such as recent myocardial infarction (within the last 90 days [41.8% versus 37.9%; $p = 0.24$]), preoperative implantation of an IABP (11.1% versus 8.4%; $p = 0.20$), and an increased rate of high-risk reoperation (1.7% versus 0.8%; $p = 0.20$) appeared to be more frequent in group A. Similarly, patients with LMD had a higher level of preoperative cardiac enzymes such as troponin-T, creatine kinase, and creatine kinase–myocardial band. The EuroSCORE (5.6 ± 3.5 versus 5.5 ± 3.6; $p = 0.96$) and the preoperative ejection fraction (56 ± 15 versus 58 ± 15; $p = 0.24$) were similar in both groups.

Intraoperative Data

In group A, the number of arterial grafts per patient was significantly higher (1.77 ± 0.95 versus 1.66 ± 0.95; $p = 0.029$) after the more frequent use of the right internal mammary artery (49.6% versus 42.3%; $p = 0.031$; Table 3). The left internal mammary artery, the radial artery, and saphenous vein grafts were used similarly frequent in both groups. In regard to saphenous vein grafts, each patient in group A received 1.95 ± 1.29 versus 1.96 ± 1.25 in group B ($p = 0.87$). Taken together, the total number of used grafts (arterial and venous) per patient was similar in both groups (3.72 ± 0.90 versus 3.62 ± 1.01; $p = 0.28$). Completeness of revascularization was achieved in 94% of patients in group A and in 95% of patients in group B ($p = 0.55$), and the completeness of revascularization index revealed no significant differences (1.44 ± 0.66 versus 1.39 ± 0.65; $p = 0.26$). Although conversion to CPB was more frequently necessary in group A (6.7% versus 5.3%; $p = 0.39$; conversion rate for whole series: 5.9%, n = 57), this failed to reach statistical significance. If converted to CPB, duration and cross-clamping time were similar in both groups.

Table 3. Intraoperative Data

Variable	Group A LMD n = 343	Group B Non-LMD n = 640	p Value
CPB conversion, n (%)	23 (6.7)	34 (5.3)	0.39
CPB time, minutes	87 ± 41	97 ± 34	0.35
Aortic cross-clamp time, minutes	70 ± 39	55 ± 10	0.44
Arterial grafts per patient	1.77 ± 0.95	1.66 ± 0.95	0.029
LIMA, n (%)	332 (96.8)	624 (97.5)	0.54
RIMA, n (%)	170 (49.6)	271 (42.3)	0.031
Radial artery, n (%)	39 (11.4)	78 (12.2)	0.76
SVG per patient	1.95 ± 1.29	1.96 ± 1.25	0.87
Use of SVG, n (%)	284 (82.8)	531 (83.0)	0.62
Total number of grafts per patient	3.72 ± 0.90	3.62 ± 1.01	0.28
Number of diseased vessels	2.77 ± 0.50	2.78 ± 0.50	0.83
Completeness of revascularization, n (%)	323 (94.2)	608 (95.0)	0.55
Completeness of revascularization index	1.44 ± 0.66	1.39 ± 0.65	0.26
EC (300 mL per unit)	2.13 ± 3.66	2.16 ± 3.49	0.64
FFP (300 mL per unit)	1.21 ± 2.76	1.19 ± 2.40	0.47
TC (300 mL per unit)	0.20 ± 0.78	0.24 ± 0.75	0.35

CPB = cardiopulmonary bypass; EC = erythrocyte concentrates; FFP = fresh frozen plasma; LIMA = left internal mammary artery; LMD = left main disease; RIMA = right internal mammary artery; SVG = saphenous vein graft; TC = thrombocyte concentrates.

Mortality, Composite Endpoint, and Logistic Regression

There was no statistical difference in regard to 30-day mortality (1.7% versus 2.2%; $p = 0.81$) and postoperative complications, such as stroke rate (0.6% versus 1.9%; $p = 0.16$; total stroke rate for whole series: 1.4%, n = 14), temporary central neurologic dysfunction (postoperative delirium) or peripheral neurologic complications (Table 4). Similarly, there were no differences in regard to postoperative increased creatinine levels (>220 μmol/L), the length of stay at the intensive care unit, and the length of hospitalization. In contrast to this, the rate of rethoracotomy was higher in group A (5.2% versus 2.7%; $p = 0.46$), but failed to reach statistical significance. In summary, all components of our composite endpoint did not show any statistical difference, and its occurrence was very similar in both groups (30.9% versus 30.8%; $p = 0.99$). Next, the logistic regression confirmed that LMD is no risk factor for the occurrence of our composite endpoint. The odds ratio was 1.00 (95% confidence interval: 0.75 to 1.33; $p = 0.99$). The result remained unchanged when the odds ratio was adjusted for the EuroSCORE.

Table 4. *Composite Endpoint and Postoperative Data*

Variable	Group A LMD n = 343	Group B Non-LMD n = 640	*p* Value
Composite endpoint (%)	106 (30.9)	198 (30.8)	0.99
Mortality (%)	6 (1.7)	14 (2.2)	0.81
IABP intraoperative (%)	1 (0.3)	9 (1.4)	0.18
CPB conversion (%)	23 (6.7)	34 (5.3)	0.39
Neurologic events (central), permanent (%)	2 (0.6)	12 (1.9)	0.16
Neurologic dysfunction (central), temporary (%)	12 (3.5)	24 (3.8)	0.52
Neurologic events (peripheral), permanent (%)	3 (0.9)	5 (0.8)	1.00
Rethoracotomy (%)	18 (5.2)	17 (2.7)	0.46
Postoperative creatinine, >220 umol/L (%)	1 (0.3)	8 (1.3)	0.17
LOS ICU >2 days (%)	61 (17.8)	131 (20.5)	0.35
Respirator time, hours	12.2 ± 12.6	12.3 ± 16.2	0.82
LOS ICU, days	2.0 ± 3.0	2.3 ± 4.2	0.55
LOS hospital, days	9.9 ± 4.6	10.3 ± 5.6	0.42
Hemoglobin, g/dL, 1 day	10.0 ± 1.5	9.9 ± 1.3	0.36
Hematocrit, %, 1 day	29.5 ± 4.3	29.0 ± 3.9	0.22
Leukocytes, 10^3/uL, 1 day	10.0 ± 3.2	9.9 ± 5.2	0.24
Thrombocytes, 10^3/uL, 1 day	164 ± 90	169 ± 94	0.79
Creatine kinase, IU/L, 1 day	455 ± 451	436 ± 495	0.24
Creatine kinase-MB, IU/L, 1 day	27 ± 32	29 ± 47	0.92
Troponin T, μg/L, 1 day	5.3 ± 16.0	5.4 ± 19.0	0.45
Creatinine, μmol/L, 1 day	87 ± 33	89 ± 49	0.98

CPB = cardiopulmonary bypass; IABP = intra-aortic balloon pump; ICU = intensive care unit; LMD = left main disease; LOS = length of stay.

Comment

In our series, it appears that OPCABG offers low mortality and an excellent clinical outcome for patients with LMD. In regard to major morbidity and mortality, we did not detect any significant differences between both groups when analyzing single outcome parameters. Furthermore, in this large population, the construction of a composite endpoint also failed to yield any difference. Logistic regression revealed an odds ratio of 1 with a narrow confidence interval and thus confirmed that LMD is no risk factor for the occurrence of the composite endpoint. Taken together, our data suggest that patients with LMD may safely undergo modern OPCABG procedures.

Many reports seem to indicate that OPCABG is associated with decreased mortality and overall complication rates [11–16], and although the OPCABG practice is being more widely accepted [22], OPCABG for high-risk patients with LMD remains controversial. Left main disease is a well-established risk factor related to cardiac adverse events [3–5], and its presence often deters a surgeon from performing OPCABG. Additionally, few data in regard to safety and outcomes of these high-risk patients are available [2, 23–27].

Our results are supported by Dewey and colleagues [23], who compared 823 patients undergoing surgical revascularization with LMD. One hundred of these patients underwent an off-pump procedure, and 723 patients underwent the conventional CABG. The authors found a mortality rate of 1% versus 4.7% (p = 0.059) in favor of OPCABG and concluded that OPCABG is a safe and feasible option for patients with LMD. In another study, Yeatman and colleagues [26] reported 387 patients undergoing either OPCABG or CABG for LMD. They displayed lower requirements for inotropes, less transfusion requirement, and a slightly shorter hospital stay, but at the price of less complete revascularization. Owing to similar mortality rates in both groups, they found OPCABG to be efficient for patients with LMD at the cost of a less complete revascularization [26]. Next, Virani and coworkers [25] compared 95 patients with LMD. Of these patients, 73 underwent OPCABG and 22 underwent revascularization using CPB. These investigators found a significantly lower number of used grafts within the OPCABG group. The mortality rate was similar, and the mean hospital length of stay was significantly lower in the OPCABG group. The authors concluded that patients with LMD can undergo OPCABG grafting safely, and suggested that LMD should no longer be seen as a contraindication to perform OPCABG [25].

In summary, these reports clearly indicate feasibility and safety of an OPCABG approach to high-risk patients with LMD. In comparison with these groups comparing OPCABG versus on-pump CABG, we focused on the important question of whether the presence of LMD affects the outcome within an OPCABG cohort. Furthermore, our subgroup with LMD was much larger than the size of the reported study populations. More similar to our study size, Lu and associates [2] evaluated 1,197 patients with LMD, of whom 259 underwent the off-pump approach versus 938 who had on-pump surgery. The authors detected comparable outcomes, but also found the OPCABG approach to be associated with significantly less complete revascularization [2].

In contrast to these reports, we were able to demonstrate completeness of revascularization as an important predictor for the long-term outcome and often reported to be a limiting factor when performing OPCABG [26, 28, 29]. Our constructed completeness of revascularization index revealed that complete revascularization was successfully achieved in almost 95% of our patients, sufficiently excluding this important risk factor. Moreover, the comparison between patients with LMD (group A) and without LMD (group B) showed no significant difference in regard to the total number of received grafts per patient and the constructed completeness of revascularization index. In contrast to other available reports [2, 23, 25, 26], our data suggest that performing OPCABG in patients with LMD was not at cost of complete revascularization in our series.

These important findings are supported by Puskas and colleagues [16] who recently demonstrated the feasibility of completeness of revascularization in OPCABG. The authors prospectively compared 200 unselected patients undergoing either OPCABG or conventional on-pump surgery. When compared with on-pump surgery, they found OPCABG to achieve similar completeness of revascularization [16]. In comparison to that study, our data show that complete revascularization is even possible in high-risk patients with LMD. This finding might be explained by our 100% standardized OPCABG approach, and especially by the vast OPCABG experience of our institution because 95% of all cases are performed in OPCABG fashion, which is far above the international average [29].

In another interesting trial, Muneretto and associates [27] prospectively compared 88 OPCABG patients and 88 on-pump patients. In their series, they were even able to highlight complete revascularization among off-pump patients by only using arterial grafts. Additionally, they found comparable mortality rates, but decreased postoperative morbidity rates among off-pump patients. They concluded that OPCABG could be successfully used for total arterial grafting without compromising the completeness of revascularization and that avoidance of cardiopulmonary bypass is associated with reduced postoperative morbidity [27].

Steed and colleagues [30] analyzed the underlying mechanisms and displayed marked subendocardial underperfusion during bypass [30]. Furthermore, Akins and associates [31] demonstrated preservation of interventricular septal function in patients having coronary artery revascularization without CPB. Taken together and as also demonstrated by the postoperative cardiac enzymatic markers (creatine kinase, creatine kinase–myocardial band, and troponin-T), which were similar in both groups, we believe that the OPCABG approach reduces myocardial stress during the procedure, hence eliminating the negative effect of LMD on outcomes.

In general, the efficacy of OPCABG surgery for high-risk patients with LMD could only be established owing to continuously improving surgical techniques and well-established intraoperative strategies. At our institution, surgical revascularization was standardized, starting with left anterior descending artery to left internal mammary artery grafting to preserve myocardial supply during cardiac torsion and proximal occlusion procedures. Then the right coronary system was approached, and finally the posterior aspect of the heart was revascularized. Furthermore, shunt insertion was done whenever possible to maintain distal perfusion during the procedure. In a prospective, randomized trial, Vassiliades and colleagues [32] recently highlighted the importance of sufficient distal perfusion during OPCABG procedures in regard to the postoperative cardiac function. Finally, our applied no-touch technique for proximal anastomosis was confirmed by a very low stroke rate for our entire series.

In conclusion, it appears that OPCABG offers a low mortality rate and excellent clinical outcome for patients requiring isolated myocardial revascularization. A modern OPCABG approach is safe and feasible for high-risk patients with LMD, and not at the cost of less complete revascularization.

Study Limitations

Of course, this is a retrospective study and all associated disadvantages apply. An ideal approach would be a trial of prospective and randomized nature. However, so far these trials are only available for OPCABG patients with a relatively low risk profile [15, 33]. Next, our results lack the force of numbers, and certainly a higher level of significance may have been obtained had we analyzed a larger cohort of patients. However, we present a homogenous population with a 100% standardized and modern approach to OPCABG. This approach is supported by at least 95% of CABG cases being done in off-pump fashion, which is far above the international standard, and also by our excellent overall outcome as well as our overall low conversion rate to CPB.

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Maximilian Emmert
Röslistrasse 8
8006 Zürich
Tl : 0041-76-2727-036
Mail : maximilian_emmert@web.de

Curriculum Vitae

Personal Details

Surname:	**Emmert**
First Name:	Maximilian
Date of Birth:	28. August 1978
Place of Birth:	Hannover
School education:	Gymnasium Sarstedt (Abitur 1998)

Current Job

05 / 2008 – lfd.	Dept. of Cardiac and Vascular Surgery University Hospital Zurich, Zurich, Switzerland (Prof. Dr. Falk)
Rotation:	
05/08 – 06/08	Outpatient Clinic Cardiac and Vascular Surgery
07/08 – 11/08	Operation Theatre Cardiac and Vascular Surgery
12/08 – 02/09	General Ward / Emergency Room
03/09 – 08/09	Intensive Care Unit Cardiac and Vascular Surgery

Medical Education

23 / 01 / 2008	Medical License
10 / 2007 – 12 / 2007	written, oral and practical exams
06 / 2007 – 08 / 2007	**Department of General Surgery** **Department of Cardiac, Thoracic and Vascular Surgery** National University Hospital / National University Singapore **Singapore** (Prof. Dr. Klima / Prof. Dr. Kofidis)
04 / 2007 – 06 / 2007	**Department of Cardiac Surgery** City Hospital Triemli Zürich **Switzerland** (Prof. Dr. Genoni)
02 / 2007 – 04 / 2007	**Department of Anaesthetics & Emergency Medicine** Royal North Shore Hospital, University of Sydney **Australia** (Consultants: Dr. MacPherson / Dr. Vinen)
12 / 2006 – 02 / 2007	**Department of Anaesthetics** Guy's & St. Thomas' Hospital, King's College London **United Kingdom** (Consultant: PD Dr. Schumacher)
10 / 2006 – 12 / 2006	**Department of Cardiology** Royal Brompton Hospital, Imperial College London **United Kingdom** (Consultant: Dr. Simon Davies)
08 / 2006 – 10 / 2006	**Dept. of Gastroenterology** (Prof. Dr. Manns) **Dept. of Pulmonology** (Prof. Dr. Welte) Hanover Medical School (MHH), **Germany**

03 / 2003 – 07 / 2006	clinical studies Hanover Medical School (MHH), Germany
04 / 2001 – 03 / 2003	pre-clinical studies University of Hamburg / University of Frankfurt, Germany

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Experimental Research

	“Characterization of Cardiac Resident Stem Cells in the Human Heart” Leibniz Research Laboratories for Biotechnology and Artificial Organs (LEBAO, Hannover Medical School, Hanover, Germany / Dept. of Cardiac, Thoracic, Transplantation and Vascular Surgery, Hannover Medical School, Hanover, Germany (Prof. Dr. Haverich / Prof. Dr. Kofidis)
05 / 2005 – 08 / 2007	experimental and statistical part
08 / 2007 – 09/2009	manuscript preparation
09 / 2009 - ongoing	submission process / manuscript under review

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Other Education

1999 – 2001	Professional Coaching A-License (Soccer) German Football Association (DFB), Frankfurt, Germany
2000 – 2001	Professional Team Management License (Soccer) German Football Association (DFB), Frankfurt, Germany

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Zürich, 7. April 2010

Publication List

1. **Emmert MY**, Salzberg SP, Felix C, Falk V
   Survival after acute and complete Occlusion of Left Main Stem
   (in press Asian Annals Cardiovascular Surgery)

2. **Emmert MY**, Emmert LS, Martinez EC, Lee CN, Kofidis T
   Off-Pump Coronary Bypass Grafting is safe and efficient in patients with severely decreased ejection fraction (<30%) ***(in press Heart Surgery Forum)***

3. **Emmert MY**, Salzberg SP, Schurr U, Reuthebuch O, Odavic D, Genoni M
   Modern off-pump coronary artery bypass grafting is safe and feasible in patients with Left Main Disease. **Ann Thorac Surg. 2010 Apr;89(4):1125-30**

4. **Emmert MY***, Salzberg S*, Schurr U, Reuthebuch O, Odavic D, Genoni M
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6. **Emmert MY**, Salzberg S, Emmert LS, Plass A, Behjati S, Felix C, Gruenenfelder J, Falk V. *Severe toxic cardiomyopathy in a female patient with Crohn`s Disease after treatment with TNF-alpha inhibitor Adalimumab.* **Eur J Heart Fail. 2009 Nov;11(11):1106-9.**

7. Salzberg S, Plass A., **Emmert MY**, Alkadhi H, Desboilles L, Grünenfelder J, Genoni M. *Left Atrial Appendage Occlusion: Early Clinical Results with a new Clip.* **J Thorac Cardiovasc Surg. 2009 Oct 30. [Epub ahead of print]**

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10. Thomas GN, Martinez EC, Woitek F, **Emmert MY**, Sakaguchi H, Muecke S, Lee CN, Kofidis T. *OPACB is safe and efficient in patients with Left Main disease and higher EuroScore.* **Eur J Cardiothorac Surg. 2009 Oct;36(4):616-20. Epub 2009 Jun 11.**

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12. Kofidis T, **Emmert MY**, Paeschke H, Emmert LS, Zhang R, Haverich A. *Long Term Follow up after MIDCABG procedure: a Multifactorial Retrospective Analysis at 1,000 pt years.* **Interact Cardiovasc Thorac Surg. 2009 Dec;9(6):990-4. Epub 2009 Sep 4.**

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